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L2: Entry 28 of 29 File: USPT Dec 31, 1991

DOCUMENT-IDENTIFIER: US 5077057 A
TITLE: Preparation of liposome and lipid complex compositions

Brief Summary Text (6):
Liposomes exhibit a wide variety of characteristics, depending upon their size, composition, and charge. For example, liposomes having a small percentage of unsaturated lipids tend to be slightly more permeable, while liposomes incorporating cholesterol or other sterols tend to be more rigid and less permeable. Liposomes may be positive, negative, or neutral in charge, depending on the hydrophilic group. For example, choline-based lipids impart a positive charge, phosphate and sulfate based lipids contribute a negative charge, and glycerol-based lipids and sterols are generally neutral in solution.

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L1: Entry 12 of 21 File: USPT Apr 6, 1999

DOCUMENT-IDENTIFIER: US 5891460 A
** **See image for Certificate of Correction** **
TITLE: Method for reducing or preventing post-surgical adhesion formation using ketotifen and analogs thereof

Abstract Text (1):

Compositions and methods for minimizing or preventing post-surgical adhesion formation between tissue, e.g., organ, surfaces in body cavities, whereby an effective therapeutic amount of anti-asthmatic ketotifen (4-1(1-methyl-4-piperidyliden-4H-benzo[4,5]cyclohepta[1,2-b] thiophene-10 (9H)-one, hydrogen fumarate salt) thereof is administered to the target injury site for a period of time sufficient to permit tissue repair. Ketotifen or analogs thereof is preferably administered in conjunction with a delivery vehicle (e.g., microcapsules, microspheres, biodegradable polymer films, lipid-based delivery systems such as liposomes and lipid foams, crystalloid and viscous instillates and absorbable mechanical barriers) useful for maintaining local concentrations of the inhibitor at the injury site at an effective level for a sustained period of time.

Brief Summary Text (39):

Another approach for the single-dose delivery of ketotifen, in accordance with the present invention, involves the use of liposomes and other lipid-based delivery systems. The encapsulation of an active agent in multilamellar vesicles (or liposomes) is a well known technique used to assist in target drug delivery and prolong drug residence. In a typical procedure, a liposome-forming powdered lipid mixture is added to the desired quantity of active agent in aqueous solution (e.g., phosphate buffered saline) to form a suspension. After a suitable hydration period, the hydrated suspension is then autoclaved to provide the liposome-active agent preparations. A lipid mixture suitable for formation of liposomes may be prepared from L-alpha-distearoyl phosphatidylcholine and cholesterol dissolved in chloroform, to which alpha-tocopherol is added; other compositions and methods for formation of liposomes would, however, also be useful for this purpose. The intraperitoneal administration of liposomes containing ibuprofen or tolmetin is described in Rodgers, K. et al., "Inhibition of Postsurgical Adhesions by Liposomes Containing Nonsteroidal Anti-inflammatory Drugs," Int. J. Fertil., Vol. 35, p. 40 (1990), the entire disclosure of which is hereby incorporated by reference.

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L1: Entry 19 of 21 File: USPT Jun 26, 1990

DOCUMENT-IDENTIFIER: US 4937254 A

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**** See image for Reexamination Certificate ****

TITLE: Method for inhibiting post-surgical adhesion formation by the topical administration of non-steroidal anti-inflammatory drug

Detailed Description Text (91):

This experiment evaluated the efficacy of a liposome/IBF combination to combat post-surgical adhesions. The procedure used was similar to that described above in Example 4 in which the treatment composition was applied to the site of surgical trauma in a single application, except that the untreated control sites in those rabbits that were given the liposome/IBF treatment were on the left-lateral peritoneal side-wall instead of being sited 1.5 to 2.0 centimeters inferior to the treatment sites in the right-lateral peritoneal side wall, and the wounding procedure described in Example 5 was used. The liposomes used in this example were DSPC/cholesterol MLV's, prepared in a manner analogous to that described above in Example 13. The treatment mixture consisted of 31 ml containing 1200 mg of MLV and 35 mg of the free acid form of IBF, suspended in 5 mM PBS. The vehicle control had the same composition, except that the IBF was omitted. Each rabbit received 10 ml of suspension, which amounted to 3.5 mg of IBF per rabbit. The treatment and vehicle control suspensions were dripped on the traumatized sites, as described above in Example 4. Three rabbits received the MLV/IBF treatment on the right side-wall site with the other site being untreated, and three rabbits received a vehicle control treatment (i.e., MLV without IBF) on the right side-wall site with no treatment on the other site. The rabbits were sacrificed 7 days post-operatively, and evaluated as described above. The results are displayed below in Table IX:

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